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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,813	REED ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11,24 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/21/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of group II, claims 8-11, 34 in paper of 11/09/04 is acknowledged.

It is noted that claim 24 is a linking claim, linking groups 1-3 and are therefore is included in group II.

Accordingly, group II, claims 8-11, 24, 34, the polypeptide of SEQ ID NO:14, are examined in the instant application.

The traverse is as follows:

1) It is not a burden for the Examiner to combine all groups I-VII together, because the search for the elected claims will include art relevant to the claims of all other groups, and because each group includes a search of the SBP1 amino acid sequence set forth as SEQ ID NO:14,

2) The divisions of claims 1-34 into seven groups would necessitate a largely duplicate effort by the USPTO and represent a noneconomical utilization of government resources, and

After review and reconsideration, claims 1-34 are subjected to a new restriction requirement, which replaces the previous restriction requirement.

RESTRICTION/ELECTION

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

Claim 24 is a linking claim, linking groups 1-3. The restriction requirement among/between the linked inventions is subject to the nonallowance of the linking claim(s), claim 24 . Upon the allowance of the linking claim(s), the restriction

requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 1, claims 1-7, 12, drawn to the nucleic acid molecules, a vector, a recombinant cell, and a method for expressing an SBP1 polypeptide, classified in class 536, subclass 23.1

Group 2, claims 8-11, 34, drawn to the SBP1 polypeptide of SEQ ID NO:14, a fragment thereof, or a chimeric protein, classified in class 530, subclass 350.

Group 3, Claims 13-16, drawn to an antibody to SEQ ID NO:14, classified in class 530, subclass 387.1.

Group 4, Claim 17, drawn to a transgenic non-human mammal expressing SEQ ID NO:13, classified in class 800, subclass 2.

Group 5, Claim 21, drawn to a method for identifying an agent that alters the association of SBP1 with a SBP1 associated polypeptide, classified in class 435, subclass 7.1.

Group 6, claims 22-23, 25, 28, drawn to a method for modulating apoptosis or or cell division or treating cancer, using the nucleic acid molecule that expresses SBP1 polypeptide, or an antisense, or a polynucleotide compound that alters the association of SBP1 with a SAP in a cell, or alters the activity of SBP1 in a cell, classified in class 514, subclass 44.

Group 7, claim 25, 28 drawn to a method for modulating apoptosis or cell division or treating cancer, using the SBP1 polypeptide, or a non-antibody polypeptide compound that alters the association of SBP1 with a SAP in a cell, or alters the activity of SBP1 in a cell, classified in class 514, subclass 2.

Group 8, claims 25, 28, drawn to a method for modulating apoptosis or cell division or treating cancer, using an antibody specific for SBP1 polypeptide, or an antibody compound that alters the association of SBP1 with a SAP in a cell, or alters the activity of SBP1 in a cell, classified in class 424, subclass 130.1.

Claim 26 is a linking claim, linking groups 9-11. The restriction requirement among/between the linked inventions is subject to the nonallowance of the linking claim(s), claim 26. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or

nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Group 9, Claims 20, 27, drawn to a method for detecting a SBP polypeptide, or diagnosing a pathology characterized by an increased or decreased level of SBP1, using an anti-SBP1 antibody, classified in class 435, subclass 7.1.

Group 10, Claim 27, drawn to a method for diagnosing a pathology characterized by an increased or decreased level of SBP1, using an SBP1 associated polypeptide, which is not an antibody, classified in class 435, subclass 7.1.

Group 11, Claims 18-19, 27, drawn to a method for detecting a SBP polynucleotide, or diagnosing a pathology characterized by an increased or decreased level of SBP1, using a SBP1 nucleic acid molecule, classified in class 435, subclass 6.

Group 12, Claims 29-31, drawn to a method for identifying a site on Survivin that interacts with SBP1, classified in class 435, subclass 7.1.

Group 13, claims 32-33, drawn to a method for identifying a compound that binds to SBP1 polypeptide, classified in class 435, subclass 7.1.

Group 14, claims 32-33, drawn to a method for identifying a compound that binds to SBP1 polynucleotide, classified in class 435, subclass 6.

Group 7 is further subject to election of a single disclosed species.

Claims 25, 28 are generic to a plurality of disclosed patentably distinct species comprising:

1) the SBP1 polypeptide, or

2) a non-antibody polypeptide compound that alters the association of SBP1 with a SAP in a cell, or alters the activity of SBP1 in a cell.

The inventions are distinct, each from the other because of the following reasons:

Inventions 1-4 as disclosed are patentably distinct products.

The polynucleotide of group I and polypeptide of group II are patentably distinct inventions for the following reasons. Polypeptides, which are composed of amino acids, and polynucleotides, which are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a polynucleotide of group I does not necessarily encode a polypeptide of group II. For example, the nucleic acid encoding SEQ ID NO:14 would not encode the chimeric protein comprising a Survivin binding domain of claim 34, such as the caspase-3 or – 7 complexed with Survivin taught by Tamm I et al, 1998, Cancer Res, 58: 5315-5320. In addition, while a polypeptide of group II can made by methods using some, but not all, of the polynucleotides that fall within the scope of group II, it can also be recovered from a natural source using by biochemical means. For instance, the polypeptide can be isolated using affinity chromatography. For these reasons, the inventions of groups I and II are patentably distinct.

Furthermore, searching the inventions of groups I and II together would impose a serious search burden. In the instant case, the search of the polypeptides and the polynucleotides are not coextensive. The inventions of Groups I and II have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is search burden also in the non-patent literature. The scope of polynucleotides as claimed extend beyond the polynucleotide that encodes the claimed polypeptides as explained above. Further, prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. As such, it would be burdensome to search the inventions of groups I and II together.

The polypeptide of group II and the antibody of group III are patentably distinct for the following reasons:

While the inventions of both group II and group III are polypeptides, in this instance the polypeptide of group II is a single chain molecule that functions as an enhancer of cyclin B1/cdc2 kinase , whereas the polypeptide of group III encompasses antibodies including IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarity determining regions (CDRs) that function to bind an epitope. Thus the polypeptide of group II and the antibody of group III are structurally distinct

molecules; any relationship between a polypeptide of group II and an antibody of group III is dependent upon the correlation between the scope of the polypeptides that the antibody binds and the scope of the antibodies that would be generated upon immunization with the polypeptide.

In this case, the polypeptide of group II is a large molecule which contains potentially hundreds of regions to which an antibody may bind, whereas the antibody of group III is defined in terms of its binding specificity to a small structure within SEQ ID NO: 14. An antibody of group III would not specifically bind all of the polypeptides of group II. For example, monoclonal antibodies to SEQ ID NO:14, having, as epitopes, a sequence from the amino acids 1-91of SEQ ID NO:14 of group II, would not bind to amino acids 85-125 of SEQ ID NO:14 of group II. Therefore the polypeptide and antibody are patentably distinct.

Furthermore, searching the inventions of group II and group III would impose a serious search burden. The inventions have a separate status in the art as shown by their different classifications. A polypeptide and an antibody which binds to the polypeptide require different searches. An amino acid sequence search of the full-length protein is necessary for a determination of novelty and unobviousness of the protein. However, such a search is not required to identify the antibodies of group III. Furthermore, antibodies which bind to an epitope of a polypeptide of group II may be known even if a polypeptide of group II is novel. In addition, the technical literature search for the polypeptide of group II and the antibody of group III are not coextensive,

e.g., antibodies may be characterized in the technical literature prior to discovery of or sequence of their binding target.

The polynucleotide of group I and the antibody of group III are patentably distinct for the following reasons. The antibody of group III includes, for example, IgG molecules which comprise 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarity determining regions (CDRs). Polypeptides, such as the antibody of group II which are composed of amino acids, and polynucleotides, which are composed of nucleic acids, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a polynucleotide of group I will not encode an antibody of group III, and the antibody of group III cannot be encoded by a polynucleotide of group I. Therefore the antibody and polynucleotide are patentably distinct.

The antibody and polynucleotide inventions have a separate status in the art as shown by their different classifications. Furthermore, searching the inventions of group I and group III would impose a serious search burden since a search of the polynucleotide of group I is would not be used to determine the patentability of an antibody of group III, and vice-versa.

The polynucleotided of group I, the polypeptided of group II and the antibodies of group III, all are distinct from and the transgenic non-human mammal for the following

reasons. The polynucleotides of group I are composed of purine and pyrimidine units, the polypeptides of group II are composed of single chain molecule comprising amino acids, and the antibodies of group III are composed of heavy and/or light chains containing constant and variable regions, whereas the transgenic animal is composed of a complex of cells, tissues and/or organs. In addition, while a polypeptide of group II can made by methods using the transgenic animal that fall within the scope of group IV, the polypeptide of group II, the polynucleotides of group I and the antibodies of group III can also be recovered from a different source. For instance, the polypeptides and the polynucleotides could be purified from natural sources, the antibodies could be made from hybridoma cell lines. For these reasons, the inventions of groups (I-III) and (IV) are patentably distinct.

Furthermore, searching the inventions of groups (I-III) and (IV) together would impose a serious search burden. In the instant case, the search of the polynucleotides, the polypeptides, the antibodies and the transgenic animal are not coextensive. The inventions of Groups (I-III) and (IV) have a separate status in the art as shown by their different classifications. Searching, for example, for the hybridizing molecules of group I, the polypeptides encoded by said hybridizing molecules of group II, and the antibodies of group III, would not be necessarily required for the search of the transgenic animal that expresses a nucleic acid molecule encoding SEQ ID NO:14 of group IV. As such, it would be burdensome to search the inventions of groups (I-III) and (IV) together.

Inventions 5-14 are materially distinct methods which differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success.

Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The instant specification does not disclose that these methods would be used together. Further, they have different objective, comprise distinct steps and/or utilize different products which demonstrates that each method has a different mode of operation. For the method for detecting SBP1 nucleic acid or a pathology, using the polynucleotide, hybridization may be used. For the method for detecting SBP1 polypeptides or a patholody, using an antibody, quantitation of labeled antibody may be used. For the method for identifying an agent that alters the association of SBP1 with a SBP1 associated protein, a gel electrophoresis or yeast hybrid system may be used. For the method of treating cancer or apoptosis or cell division, a polynucleotide or a polypeptide or an antibody may be administered into a patient. For identifying sites on Survivin that interact with SBP1, mutants of Survivin may have to be constructed. For identifying compounds that bind to SBP1 polypeptide or polynucleotides, mass spectrometry or NMR or virtual computational methodology may be used.

Therefore, each method is divergent in objectives, and/or materials and steps. For these reasons the Inventions 5-14 are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. The inventions of Groups 5-14 have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search the inventions of Groups 5-14 together.

The inventions of Groups (1) and (6, 11, 14) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case the nucleic acid molecule can be used for making recombinant proteins, as opposed to its use in treating cancer.

The inventions of Groups (2) and (5, 7-10, 12-13) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case the polypeptide can be used for making antibodies, as opposed to its use treating cancer.

The inventions of Groups (3) and (8, 9) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially

different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case the antibody product as claimed can be used in a materially different process such as affinity chromatography, as opposed to its use in treating cancer.

The inventions of Groups (1) and (5, 7-10, 12-13, 15) are not at all related because the nucleic acid of Group I is not used in any of the methods of Groups 5, 7-10, 12-13, 15.

The inventions of Groups (2) and (6, 11, 14) are not at all related because the polypeptide of Group 2 is not used in any of the methods of Groups 6, 11, 14.

The inventions of Groups (3) and (5-7, 10-14) are not at all related because the antibody of Group 3 is not used in any of the methods of Groups 5-7, 10-14.

The inventions of Groups (4) and (5-14) are not at all related because the transgenic mammal of Group 4 is not used in any of the methods of Groups 5-14.

The species are distinct, because they structurally distinct.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and/or recognized divergent subject matter, and because the searches for different groups are not co-extensive, and it would be an undue experimentation of the Examiner to search all the groups together, restriction for examination purposes as indicated is proper (see MPEP 806.04(a)-806.04(i), 808.01(a), 808.02, 806.05-806.05(i)).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one

claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above

policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

It is noted that in the new restriction requirement, group II is directed to the same elected invention. A confirmation of the elected invention in a reply to this Office action however is required.

Accordingly, group II, claims 8-11, 24, 34, the polypeptide of SEQ ID NO:14, are examined in the instant application.

OBJECTION

1. The specification is objected to, because it contains empty spaces, for example, on page 1, first paragraph.

2. Claims 8-11are objected to, because they are dependent on non-elected claim 1.

3. Claims 8-11 are objected to, for the apparent typographic error "encoding" in claim 8, and it is apparent that the term "encoded" is the proper term.

4. Claim 34 is objected to for the use of the language "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain, as the sole means of identifying the claimed protein fragment, because different laboratories may use the same laboratory designations to define completely distinct protein fragments. Amendment of the claim to

include physical and/or functional characteristics of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory domain" which unambiguously define "a Survivin binding domain", and "a cyclin-dependent kinase regulatory domain" is required.

REJECTION UNDER 35 USC 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 34 is rejected under 35 USC 101 because the claim is directed to non-statutory subject matter, because the specification does not define the term chimeric and it reads on endogenous proteins (see 102 rejection below).

The chimeric protein as claimed has the same characteristics and utility as a chimeric protein found naturally and therefore does not constitute patentable subject matter. In the absence of the hand of man, the naturally occurring polypeptide is considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Amendment of the claims to recite " an isolated chimeric protein" is suggested to overcome this rejection.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 8, 24, 34 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claim 8 is drawn to an isolated SBP1 polypeptide, or "functional fragment" thereof, encoded by a nucleic acid molecule that encodes an SBP1 polypeptide or "functional fragment" thereof, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, and wherein said nucleic acid molecule "hybridizes to the complement" of a) a nucleic acid molecule encoding a polypeptide comprising amino acids 1-91 of SEQ ID NO:14, b) a nucleic acid molecule encoding a polypeptide comprising amino acids 85-125 of SEQ ID NO:14, or c) a nucleic acid molecule encoding SEQ ID NO:14.

Claim 24 is drawn to a therapeutic composition, comprising a pharmaceutically acceptable carrier and a SBP polypeptide or a functional fragment thereof.

Claim 34 is drawn to a chimeric protein comprising a "SBP1" domain, selected from the group consisting of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain.

The specification discloses that SBP refers to novel members of the Cks/Suc family of proteins, wherein said SBP comprises a Survivin-binding domain (p.8, lines 18-

20). The specification further discloses that the term "SBP" refers to substantially pure native SBP, or "naturally occurring allelic variants" thereof (p.8, lines 26-29). The specification discloses that in "another embodiment" SBPs referred herein, are those polypeptides recognized by an antibody that also specifically recognizes "a SBP", "including" SEQ ID NO:2 or 14 (p.9, first paragraph).

The specification discloses that the amino acids 1-90 of the SBP1 polypeptide of SEQ ID NO:14 is necessary for binding to Survivin (Example 7, on pages 71-72). The specification further discloses that a mutation of SBP1, wherein the residues 102-142 are deleted, eliminates the possible cyclin dependent kinase regulatory domain (RS) (p.72, lines 2-5).

The specification discloses alignment of cyclin dependent kinase regulatory domain (RS) of SBP1(amino acids 85-125 of SEQ ID NO:14) with RS domain of other known proteins, human Cks1, human Cks2, Drosophila Cks1 and Yeast Cks1 (figure 3 legend on page 7).

It is noted that in view of the definition of SBP, the language "SBP" polypeptide or "SBP1" polypeptide alone, without being accompanied by a recitation that said SBP is SEQ ID NO: 14, encompasses variants of the SBP of SEQ ID NO:14.

It is further noted that a complement could be a partial or complete complement, wherein a partial complement could share with the claimed sequences only a few complementary nucleotides.

In addition, other than the amino acids 1-90 and 85-125 of SEQ ID NO:14, which are responsible for Survivin binding, and regulation of cyclin-dependent kinase,

respectively, the specification does not disclose which other domains or fragment of SEQ ID NO:14, that confer myriads of possible function of SEQ ID NO:14, in view that the definition of "functional" in the specification is non-limiting.

Claim 8 encompasses a "functional "fragment of SEQ ID NO:14, wherein said fragment has undefined functions, and the structure of said fragment is not disclosed. There is no correlation between the undefined functions and structure.

Claim 8 also encompasses a variant of the full length SBP1 of SEQ ID NO:14 or fragment thereof, encoded by a nucleic acid molecule that hybridizes under highly stringent conditions to the complement of nucleic acid encoding SEQ ID NO:14, or a fragment thereof, wherein **said complement has one or a few nucleotides complementary to the nucleic acid encoding SEQ ID NO:14 or a fragment thereof,** wherein said variant binds Survivin or enhance cyclin B1/cdc2 kinase, and **wherein the structure of said variant or of the complement to which the nucleic acid encoding said variant is hybridized to is not disclosed in the specification.**

In other words, claim 8 encompasses unknown sequences that binds Survivin, or that have the function of enhancing cyclin B1/cdc2 kinase, wherein the nucleic acid molecules encoding said sequences hybridize under highly stringent conditions to its own complementary sequence or a sequence that is unrelated to the nucleic acid encoding SEQ ID NO:14..

Claim 24 encompasses a variant of SEQ ID NO:14, with unknown structure.

Claim 34 encompasses a chimeric protein comprising a domain of a variant of the SBP1 of SEQ ID NO:14, wherein said domain is a variant Survivin-binding domain, and wherein the structure of said variant domain is not disclosed in the specification.

In addition, it is noted that **the specification only discloses a single species of SBP1 polypeptide of SEQ ID NO:14, and a single species of the SBP1 Survivin binding domain, i.e. amino acids 1-90 of SEQ ID NO:14.**

There is no disclosure of a common structure for the functional fragment, the variant of the full length of SEQ ID NO:14, or the chimeric protein comprising the variant Survivin binding domain. There is no disclosure of the consensus sequence for the domain that binds to Survivin or that enhances cyclin B1/cdc2 kinase

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that [a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials. Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as vertebrate insulin cDNA or mammalian insulin cDNA without more, is not an adequate written description of the

> genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. **A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is** (emphasis added).

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V: Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying

characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of a SBP polypeptide, or a functional fragment of SBP1, or a SBP1 polypeptide encoded by the hybridizing polynucleotide, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, or a Survivin binding domain, as shown by the example per Lilly, by structurally describing a representative number of a SBP polypeptide, or a functional fragment of SBP1, or polypeptides encoded by the hybridizing polynucleotides, wherein said polypeptides bind Survivin or enhance cyclin B1/cdc2 kinase activity, or Survivin binding domains or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, as shown in the example per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe a SBP polypeptide, or a functional fragment of SBP1, or a SBP1 polypeptide encoded by the hybridizing

polynucleotide, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, or a Survivin binding domain in a manner that satisfies 112, first paragraph, written description requirement, as exampled in either the Lilly or Enzo standards. The specification does not provide the complete structure of a SBP polypeptide, or a functional fragment of SBP1, or a SBP1 polypeptide encoded by the hybridizing polynucleotide, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, or a Survivin binding domain, other than SEQ ID NO:14, and amino acids 1-90, 85-125 of SEQ ID NO:14, nor any physical or chemical characteristics of a SBP polypeptide, or a functional fragment of SBP1, or a SBP1 polypeptide encoded by the hybridizing polynucleotide, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, or a Survivin binding domain, other than SEQ ID NO:14, and amino acids 1-90, 85-125 of SEQ ID NO:14, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single polypeptide of SEQ ID NO:14, and amino acids 1-90, 85-125 of SEQ ID NO:14, this does not provide a description of a SBP polypeptide, or a functional fragment of SBP1, or a SBP1 polypeptide encoded by the hybridizing polynucleotide, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, or a Survivin binding domain that would satisfy the 112, first written description requirment, as exemplified by the standard set out in Enzo.

The specification also fails to describe a SBP polypeptide, or a functional fragment of SBP1, or a SBP1 polypeptide encoded by the hybridizing polynucleotide, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, or a

Survivin binding domain, as required by the 112, first paragraph, written description, as exemplified by the test set out in Lilly. The specification describes only a single a single polypeptide of SEQ ID NO:14, and amino acids 1-90, 85-125 of SEQ ID NO:14. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of a SBP polypeptide, or a functional fragment of SBP1, or a SBP1 polypeptide encoded by the hybridizing polynucleotide, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, or a Survivin binding domain, that is required to practice the claimed invention, and one would conclude that the invention did not have possession of the claimed SBP polypeptide, or functional fragment of SBP1, or the claimed polypeptide encoded by the hybridizing polynucleotide, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, or the claimed Survivin binding domain.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated SBP1 polypeptide of SEQ ID NO:14, or a polypeptide consisting of a fragment of SEQ ID NO:14, wherein said fragment comprises amino acids 1-91 or 85-125 of SEQ ID NO:14, **does not reasonably provide enablement for 1) a SBP polypeptide, 2) a "functional fragment" of SBP1**

polypeptide, or 2) a SBP1 polypeptide, or "functional fragment" thereof, encoded by a nucleic acid molecule that encodes an SBP1 polypeptide or "functional fragment" thereof, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, and wherein said nucleic acid molecule "hybridizes to the complement" of a) a nucleic acid molecule encoding a polypeptide comprising amino acids 1-91 of SEQ ID NO:14, b) a nucleic acid molecule encoding a polypeptide comprising amino acids 85-125 of SEQ ID NO:14, or c) a nucleic acid molecule encoding SEQ ID NO:14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claim 8 is drawn to an isolated SBP1 polypeptide, or "functional fragment" thereof, encoded by a nucleic acid molecule that encodes an SBP1 polypeptide or "functional fragment" thereof, wherein said polypeptide binds Survivin or enhances cyclin B1/cdc2 kinase activity, and wherein said nucleic acid molecule "hybridizes to the complement" of a) a nucleic acid molecule encoding a polypeptide comprising amino acids 1-91 of SEQ ID NO:14, b) a nucleic acid molecule encoding a polypeptide comprising amino acids 85-125 of SEQ ID NO:14, or c) a nucleic acid molecule encoding SEQ ID NO:14.

It is noted that in view of the definition of SBP, supra, the language "SBP" polypeptide or "SBP1" polypeptide alone, without being accompanied by a recitation that said SBP is SEQ ID NO: 14, encompasses variants of the SBP of SEQ ID NO:14.

It is further noted that a complement could be a partial or complete complement, wherein a partial complement could share with the claimed sequences only a few complementary nucleotides.

In addition, other than the amino acids 1-90 and 85-125 of SEQ ID NO:14, which are responsible for Survivin binding, and regulation of cyclin-dependent kinase, respectively, the specification does not disclose which other domains or fragments of SEQ ID NO:14, that confer myriads of possible function of SEQ ID NO:14, in view that the definition of "functional" in the specification is non-limiting.

Claim 8 encompasses "functional "fragments of SEQ ID NO:14, wherein said fragment could confer any of myriads of function of SEQ ID NO:14.

Claim 8 also encompasses a variant of the full length SBP1 of SEQ ID NO:14 or fragment thereof, encoded by a nucleic acid molecule that hybridizes under highly stringent conditions to the complement of nucleic acid encoding SEQ ID NO:14, or a fragment thereof, wherein **said complement has one or a few nucleotides complementary to the nucleic acid encoding SEQ ID NO:14 or a fragment thereof,** wherein said variant binds Survivin or enhance cyclin B1/cdc2 kinase, and **wherein the structure of said variant or of the complement to which the nucleic acid encoding said variant is hybridized to is not disclosed in the specification.**

In other words, claim 8 encompasses unknown sequences that binds Survivin, or that have the function of enhancing cyclin B1/cdc2 kinase, wherein the nucleic acid molecules encoding said sequences hybridize under highly stringent conditions to its

own complementary sequence or a sequence that is unrelated to the nucleic acid encoding SEQ ID NO:14..

There is no disclosure of the consensus sequence for the domain that binds to Survivin, or that enhances cyclin B1/cdc2 kinase.

One cannot extrapolate the teaching in the specification to the claims, because one would not know how to make the claimed functional fragment, in view that said functional fragment could confer any of myriads of function of SEQ ID NO:14, and further in view that there is no teaching in the specification which fragments that confer any of myriads of function of SEQ ID NO:14.

Further, one cannot extrapolate the teaching in the specification to the claims, because it would be undue experimentation for screening from myriads of polynucleotides hybridizing to a sequence that has in common with SEQ ID NO:14 only one or some complementary nucleotides, those that encode a polypeptide that binds Survivin or enhances cyclin B1/cdc2 kinase, and consequently it would be undue experimentation for one of skill in the art to make the claimed polypeptide encoded by said polynucleotides.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

2. Claim 24 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising the polypeptide of SEQ ID NO:14 in a pharmaceutically acceptable carrier, **does not reasonably provide enablement for a "therapeutic composition" comprising a SBP polypeptide**. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claim 24 is drawn to a "therapeutic composition" comprising a SBP polypeptide in a pharmaceutically acceptable carrier.

The specification discloses isolated nucleic acids encoding survivin binding protein (SBPs) or SEQ ID NO:14, (p.5,lines 8-9), that enhances cyclin B1/cdc 2 kinase activity (Example 8 on pages 72-73). The specification discloses that Survivin, a member of the inhibitor of apoptosis proteins, such as the apoptosis protein capase-3 or-7, is phosphorylated by cdc2/cyclin (p.2, 4). The specification discloses that the function of SBP is a modulator of the apoptosis inhibitor Survivin (p.9, second paragraph).

The specification contemplates the use of the claimed polypeptide in induction of apoptosis or as tumor suppressor, such as for targeting to a tumor to induce apotosis (page 32-34) for example, by decreasing the SBP activity (p.57, last paragraph to p.59).

One cannot extrapolate the teaching in the specification to the scope of the claim. It is unpredictable that the claimed SBP polypeptide could be useful for inducing apoptosis or for treating cancer, due to possible homeostasis, and because cancer treatment is unpredictable. It is well known in the art that there exists several apoptosis antagonists, such as members of the Bcl-2 family and CrmA that act upstream of the effector caspase-3 and-6, e.g. inhibition of the activation of the initiator caspase-9 (Colussi, PA et al, 1998, J Biol Chem, 273(41): 26566-26570, especially p.26569, first

column). Gottschalk, AR et al, 1996, Cell Death and Differentiation, 3(1): 113-118, teach that overexpression of BAR, a well known apoptosis promoter, although can inhibit Bcl-2 from prolonging cell survival upon growth factor withdrawl, does not inhibit Bcl-XL from preventing apoptosis in a cell line WEHI-231. Gottschalk, AR et al further teach that regulation of a cell's apoptotic threshold is likely to result from a complex set of interactions among Bcl-2 family members and other, as yet uncharacterized, regulators of apoptosis. Thus, apoptosis is a complex phenomenon, wherein there are diverse cell death pathways, which depend on cell type and cell death stimulus (Vogel MW et al, 2002, Cerbellum, 1(4): 277-87), wherein apoptosis could be regulated by homeostasis mechanisms. In another example, Xu Xin et al, 2001, FASEB J, 15(4): A313, teach that compensatory mechanism could regulate apoptosis to overcome the low induction of Fas and FasL in activated CD4+ cells of IRF-1 null mice. In addition, homeostasis is a common phenomena, as taught by for example, Hummler E et al, 1994, PNAS, USA, 91: 5647-5661. Hummler et al teach that there is compensation within the CREB/ATF family of transcription factors, wherein mice with disruption of the CREB gene appear to be healthy, and has an increase level of CREM, another member of the CREB/ATF family , and no change in the level of ATF1. Hummler E et al conclude that CREB is not the sole mediator of camp-dependent transcriptional regulation, and probably acts in concert with a specific subset of camp responsive element-binding proteins to transduce the camp signal and in its absence, these same protein can compensate for CREB function. Thus, regulation of apoptosis is a complex phenomena, and one cannot

predict whether homeostasis would prevent the use of claimed SBP polypeptide in inducing apoptosis, such as via reduction of the activity of the claimed SBP polypeptide.

Further, one cannot extrapolate the teaching of the specification to the scope of the claims because it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable, for example, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical

barriers to drug delivery in tumors is a work in progress (p. 36, col 2). In addition, Hartwell et al (Science, 1997, 278:1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells, that most anticancer drugs have been discovered by serendipity and that the molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (para bridging pages 1064-1065) and Jain (cited supra) specifically teaches that systemic treatment typically consists of chemotherapeutic drugs that are toxic to dividing cells (p. 58, col 2, para 2).

Thus, due to the unpredictability of cancer therapy, one cannot predict whether the claimed SBP polypeptide would be effective for use in inducing apoptosis in cancer, such as via reduction of the activity of the claimed SBP polypeptide.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

3. Claim 34 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting of a domain of SEQ ID NO:14, selected from the group consisting of amino acids 1-90, which binds to Survivin, and amino acids 85-125 of SEQ ID NO:14, which regulates cyclin-dependent kinase 2, and a heterologous protein comprising said domain, **does not reasonably provide enablement for a chimeric protein comprising a "SBP1" domain, selected from the group consisting of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain.** The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claim 34 is drawn to a chimeric protein comprising a "SBP1" domain, selected from the group consisting of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain.

Claim 34 encompasses myriads of unrelated sequences, that are attached to a Survivin binding domain or a cyclin-dependent kinase regulatory domain; as exampled by some of the sequences, which are known in the art, for example caspase-3 or -7 (see 102 rejection), and having completely different characteristics and properties than SEQ ID NO:14.

The specification does not disclose how to make the claimed chimeric molecules, such that they have the characteristics or properties of SEQ ID NO:14.

One cannot extrapolate the teaching in the specification to the scope of the claims, because it is well known in the art that protein chemistry is probably one of the most unpredictable areas of biotechnology and that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. For example, Bowie et al (Science, 1990, 257 : 1306-1310) teach that an amino acid sequence encodes a message that determine the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instruction of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted

structural determinations to ascertain functional aspects of the protein is extremely complex (col.1, p.1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitution can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col.2, p.1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al, (Journal of Cell Biology, 1990, 11: 2129-2138), who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. The Journal of Immunology, 1989, 143(8): 2595-2601, and Gillies et al. Human Antibodies and Hybridomas, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

The specification does not disclose how to make the claimed nucleic acid molecules, such that they would function or have the properties as claimed.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

REJECTION UNDER 35 USCS 102(b or e)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Tamm I et al, 1998, Cancer Res, 58: 5315-5320.

Claim 34 is drawn to a chimeric protein comprising a "SBP1" domain, selected from the group consisting of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain.

Tamm et al teach that Survivin binds to active caspase-3 and –7.

The complex of Survivin-caspase-3 or –7 seems to be the same as the claimed chimeric protein, since it would comprise a domain of caspase-3 or 7 that binds to Survivin.

Although the reference does not specifically teach that the complex of Survivin-caspase comprises a "SBP1 domain", however, the claimed chimeric protein appears to be the same as the prior art complex of Survivin-caspase. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

2. Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Bourne, Y et al, 1996, Cell, 84: 863-874, or Tsai, LH et al, 1994, Nature, 371 (6496): 419-423.

Claim 34 is drawn to a chimeric protein comprising a "SBP1" domain, selected from the group consisting of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain.

The specification discloses the cyclin-dependent kinase regulatory subunit domains of known proteins, such as human Cks1, Cks2, and their homology to the cyclin-dependent kinase regulatory domain (amino acids 85-125) of the claimed SBP1 of SEQ ID NO:14 (figures 2-3).

Bourne et al teach a complex of Ckshs1(human cks1, abstract lines 1-4) and the cyclin dependent kinase 2 (cdk2). Bourne et al teach that CKsHs1 binds to the kinase via all four beta strands (abstract and figure 3 on page 867), and that said interaction is essential for cell cycle progression (p.868, first column, under mutational analysis of the CDK2-CKsHs1 interface, bridging second column). Bourne et al further teach that Cks targets the active Cdk to its substrates or other regulatory proteins (p.871, second column, first paragraph).

Tsai et al teach that p35 is a regulatory subunit of cyclin-dependent kinase 5 and associates physically with Cdk5 in vivo and activates the Cdk5 kinase (abstract).

The complex taught by Bourne et al or Tsai et al seem to be the same as the claimed chimeric protein, comprising a domain that regulates a cyclin-dependent kinase.

Although the reference does not specifically teach that the complex comprises a "SBP1 domain", however, the claimed chimeric protein appears to be the same as the prior art complex. The office does not have the facilities and resources to provide the

factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

3. Claims 8-11 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 200142451-A2.

Claims 8-11 are drawn to:

1) An isolated SBP1 polypeptide or functional fragment thereof, encoded by an isolated nucleic acid molecule encoding an SBP1 polypeptide or functional fragment thereof, selected from the group consisting of:

a) a nucleic acid encoding a polypeptide "comprising" amino acids 1-91 or SEQ ID NO:14, wherein said polypeptide binds Survivin,

b) a nucleic acid molecule encoding a polypeptide comprising amino acids 85-125 of SEQ ID NO:14, wherein said polypeptide enhances cyclin B1/cdc2 kinase activity,

c) a nucleic acid molecule encoding SEQ ID NO:14, and

d) a nucleic acid molecule that encodes a polypeptide that binds Survivin or enhances cyclin B1/cdc2 kinase activity, wherein said nucleic acid molecule "hybridizes to the complement" of a) a nucleic acid molecule encoding a polypeptide comprising amino acids 1-91 of SEQ ID NO:14, b) a nucleic acid molecule encoding a polypeptide

comprising amino acids 85-125 of SEQ ID NO:14, or c) a nucleic acid molecule encoding SEQ ID NO:14 (claim 8).

2) The SBP1 polypeptide of claim 8, wherein said polypeptide "comprises" amino acids 1-91, or 82-125 of SEQ ID NO:14, or SEQ ID NO:14 (claims 9-11).

WO 200142451-A2 teaches a polynucleotide encoding a polypeptide and a biologically active fragment thereof (claim 1). Under MPSRCH sequence similarity search, the polynucleotide sequence taught by WO 200142451-A2 is 100% similar to the full length SEQ ID NO:13, from nucleotide 1 to nucleotide 492 (MPSRCH search report, 2005, us-10-057-813-13.rng, pages 3-4). The encoded protein taught by WO 200142451-A2 is 100% similar to the full length SEQ ID NO:14, from amino acid 1 to amino acid 163 (MPSRCH search report, 2005, us-10-057-813-14.rag, pages 1-2).

Thus the polypeptide and a biologically active fragment taught by taught by WO 200142451-A2 seem to be the same as the claimed polypeptide and functional fragment thereof.

Although the reference does not specifically teach that the polypeptide is a SBP1 polypeptide, or that the polypeptide binds Survivin, or enhances cyclin B1/cdc2 kinase activity, however, the claimed polypeptide and functional fragment thereof appears to be the same as the prior art polypeptide and biologically active fragment thereof. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed

product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

REJECTION UNDER 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 200142451-A2, supra, in view of Johnstone and Thorpe (Immunochemistry in Practice, 2nd Ed., 1987, Blackwell Scientific Publications, Oxford, pages 49-50)

Claim 24 is drawn to a therapeutic composition comprising a pharmaceutically acceptable carrier and a SBP polypeptide.

Claim 24 recite the claimed SBP polypeptide, formulated as "a therapeutic composition". However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claim 24 reads on the ingredient per se, which is SBP polypeptide.

The teaching of WO 200142451-A2 has been set forth above. Briefly, the polypeptide taught by WO 200142451-A2 seems to be the same as the claimed SBP1 polypeptide of SEQ ID NO:14, supra, although WO 200142451-A2 does not teach that the polypeptide is a SBP polypeptide and comprising a "SBP1" domain, selected from

the group consisting of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain.

In addition WO 200142451-A2 teaches that the polypeptide could be used for prevention, treatment and diagnosis of diseases associated with inappropriate Genset gene expression (paragraph under use in the abstract).

WO 200142451-A2 does not teach a pharmaceutically acceptable carrier.

Johnstone and Thorpe teach that compositions of antibodies are stored in phosphate buffer saline, which is considered to be an acceptable carrier for storage of antibodies, because Johnstone and Thorpe teach that antibodies could be damaged, even though antibodies are robust proteins, and that antibodies are happiest in neutral isotonic buffers such as PBS (p.50, first paragraph).

It is noted that a pharmaceutically acceptable carrier could be interpreted as any type of carrier, such as buffer, provided that it is pharmaceutically acceptable.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to put the polypeptide taught by WO 200142451-A2 in buffer, such as phosphate buffer saline (PBS), because of the following reasons: 1) Johnstone and Thorpe teach that compositions of antibodies are stored in phosphate buffer saline, which is considered to be an acceptable carrier for storage of antibodies, because Johnstone and Thorpe teach that antibodies could be damaged, even though antibodies are robust proteins, and that antibodies are happiest in neutral isotonic buffers such as PBS (p.50, first paragraph), and 2) Antibodies are proteins and it was conventional to store proteins in phosphate buffer saline. One of ordinary skill would

have been motivated to do so in order to develop compositions suitable for storage, with a reasonable expectation of success.

2. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 200142451-A2, supra, in view of US Patent No. 5,968,781.

Claim 34 is drawn to a chimeric protein comprising a "SBP1" domain, selected from the group consisting of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain (claim 34).

The teaching of WO 200142451-A2 has been set forth above. Briefly, the polypeptide taught by WO 200142451-A2 seems to be the same as the claimed SBP1 polypeptide of SEQ ID NO:14, supra. Although WO 200142451-A2 does not teach that the polypeptide is a SBP polypeptide and comprising a "SBP1" domain, selected from the group consisting of "a Survivin binding domain", and "a cyclin-dependent kinase regulatory" domain, one would have expected that the polypeptide taught by WO 200142451-A2 would be a SBP polypeptide and would comprise a "SBP1" domain, selected from the group consisting of "a Survivin binding domain" ", and "a cyclin-dependent kinase regulatory" domain.

In addition WO 200142451-A2 teaches that the polypeptide could be used for prevention, treatment and diagnosis of diseases associated with inappropriate Genset gene expression (paragraph under use in the abstract).

WO 200142451-A2 does not teach a chimeric protein.

US Patent No. 5,968,781 teaches a recombinant molecule comprising a polynucleotide encoding a protein which further comprises nucleotide sequences

encoding a histidine tag inserted into the 5' terminus or 3' terminus of the gene. US Patent No. 5,968,781 further teaches that the tag prevents degradation of the recombinant protein and facilitates purification of the protein by histidine tag affinity column as a metal chelating affinity column (col 3, lines16-25).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the methods US Patent No. 5,968,781 to produce a recombinant protein taught by WO 200142451-A2 with a histidine tag because histidine tags are conventionally used to facilitate purification of the recombinant protein. One of ordinary skill in the art at the time the invention was made would have been motivated to use the methods of US Patent No. 5,968,781 in order to produce an easily recovered expressed polypeptide and in order to make a stabilized protein in solution. One of ordinary skill in the art would be motivated to make the chimeric protein with a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS

February 01, 2005

SUSAN UNGAR, PH.D
PRIMARY EXAMINER